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DATE: Monday, April 10, 2006

Hide?	Set Name	Query	Hit Count
		DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR	
☐	L11	l6 and prion	4
☐	L10	l6 and sup$6	97
☐	L9	l6 and L8	13
☐	L8	(prion or amyloid)	16345
☐	L7	L6 and chimeric	108
☐	L6	l4 and L5	299
☐	L5	@ay<=1998	17356954
☐	L4	(protein$2 or peptide$2) same (aggregat$8) same (cerevisiae or yeast)	780
		DB=USPT; PLUR=YES; OP=OR	
☐	L3	(protein$2 or peptide$2) same (aggegat$8) same (cerevisiae or yeast)	0
☐	L2	(protein$2 or peptide$2) same (aggegat$8) same (in adj3 yeast)	0
		DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR	
☐	L1	((aggregat$8 same (intracell$6 or (in adj vivo) or cell$8)) and ((((@ay<=1998) and ((assay$8 or screen$8 or test$8) same (aggregat$8) same (prion or amyloid$8) and (yeast or cerevisiae)))))	16

END OF SEARCH HISTORY

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DATE: Monday, April 10, 2006

Hide?	Set Name	Query	Hit Count
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☐	L11	l6 and prion	4
☐	L10	l6 and sup$6	97
☐	L9	l6 and L8	13
☐	L8	(prion or amyloid)	16345
☐	L7	L6 and chimeric	108
☐	L6	l4 and L5	299
☐	L5	@ay<=1998	17356954
☐	L4	(protein$2 or peptide$2) same (aggregat$8) same (cerevisiae or yeast)	780
		DB=USPT; PLUR=YES; OP=OR	
☐	L3	(protein$2 or peptide$2) same (aggegat$8) same (cerevisiae or yeast)	0
☐	L2	(protein$2 or peptide$2) same (aggegat$8) same (in adj3 yeast)	0
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☐	L1	((aggregat$8 same (intracell$6 or (in adj vivo) or cell$8)) and ((((@ay<=1998) and ((assay$8 or screen$8 or test$8) same (aggregat$8) same (prion or amyloid$8) and (yeast or cerevisiae)))))	16

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 s yeast and aggregat? and protein? and prion
         89281 YEAST
         19794 YEASTS
         99306 YEAST
                 (YEAST OR YEASTS)
        116375 AGGREGAT?
       1961054 PROTEIN?
          5738 PRION
          4801 PRIONS
          7162 PRION
                 (PRION OR PRIONS)
L1         110 YEAST AND AGGREGAT? AND PROTEIN? AND PRION

=> s l1 and py<1998
      11488813 PY<1998
                 (PY<19980000)
L2            8 L1 AND PY<1998

=> d bib ab 1-
YOU HAVE REQUESTED DATA FROM 8 ANSWERS - CONTINUE? Y/(N):y

L2   ANSWER 1 OF 8     MEDLINE on STN
AN   1998242470     MEDLINE
DN   PubMed ID: 9581369
TI   [Prions and the problems they raise].
     Les prions et les problemes qu'ils posent.
AU   Burny A
CS   Faculte universitaire des Sciences agronomiques de Gembloux.
SO   Bulletin et memoires de l'Academie royale de medecine de Belgique,
     (1997) Vol. 152, No. 6, pp. 247-63.
     Journal code: 7608462. ISSN: 0377-8231.
CY   Belgium
DT   Journal; Article; (JOURNAL ARTICLE)
LA   French
FS   Priority Journals
EM   199806
ED   Entered STN: 19980708
     Last Updated on STN: 19980708
     Entered Medline: 19980619
AB   A prion is an "infectious" protein.  Most probably,
     prions play a major role, direct or indirect, in the propagation
     of neurodegenerative diseases such as spongiform encephalopathies.  By
     extension, the term prion is also used to explain several cases
     of dominant cytoplasmic heredity known in the yeast
     Saccharomyces cerevisiae.  Several recent publications, briefly discussed,
     suggest that amyloid fibrils (aggregated prions)
     appear late in some experimental neuropathies, long after the disease
     symptoms.  The present uncertainty deals with the presence or not of a
     second component besides the prion to make up the infections
     agent.  As such, the prion theory raises major problems about
     the chemistry of protein folding.  A major contribution in
     prion research is urgent and mandatory.

L2   ANSWER 2 OF 8     MEDLINE on STN
AN   1998121249     MEDLINE
DN   PubMed ID: 9461351
TI   Long non-stop reading frames on the antisense strand of heat shock
     protein 70 genes and prion protein (PrP) genes
     are conserved between species.
AU   Rother K I; Clay O K; Bourquin J P; Silke J; Schaffner W
CS   Institut fur Molekularbiologie II, Universitat Zurich, Switzerland.
SO   Biological chemistry, (1997 Dec) Vol. 378, No. 12, pp. 1521-30.
     Journal code: 9700112. ISSN: 1431-6730.
CY   GERMANY: Germany, Federal Republic of
```

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-J01104; GENBANK-J02579; GENBANK-M11717; GENBANK-M20567; GENBANK-M76613; GENBANK-U09861; GENBANK-X12926
EM 199803
ED Entered STN: 19980326
Last Updated on STN: 19980326
Entered Medline: 19980318
AB Several mammalian genes, including heat shock **protein** (Hsp70) and **prion protein** (PrP) genes, have been reported to have long open reading frames (ORFs) or non-stop reading frames (NRFs) in the antisense direction. A simple explanation would be that these long antisense reading frames, which are usually in the same triplet frame as the coding strand, are the fortuitous byproduct of a high overall [G+C] content with concomitant preference for G/C over A/T in the third codon position, a preference for RNY type codons (purine/any nucleotide/pyrimidine), and/or a bias against serine and leucine, the only amino acids with codons that can be read as stop codons in the antisense direction. The PrP genes and most heat shock genes with long antisense NRFs (aNRFs) are indeed relatively [G+C] rich but do not show a bias against serine and leucine. In several vertebrates investigated, at least one of the Hsp70 genes has a long antisense reading frame, and we found that some, though not all, putative stop codons in long Hsp70 antisense reading frames were due to sequencing errors. The PrP gene contains an extended antisense open reading frame in all 45 eutherian mammals tested, but not in a marsupial and in a bird. In the PrP gene, the long, **protein**-coding exon also harbors the antisense nonstop reading frame. In both Hsp70 and PrP genes, the putative antisense **protein** sequence is well conserved. Even though there is no clear evidence in Hsp70 or PrP genes for the existence of the respective antisense **proteins**, we speculate that such antisense **proteins** serve to regulate the genuine Hsp and PrP **proteins** under special circumstances. Alternatively, regulation might occur at the RNA level, and the antisense RNA would merely lack stop codons to prevent its rapid degradation by an mRNA quality control mechanism that is triggered by premature stop codons. We note that both Hsp and PrP are involved in physiological or pathological **protein aggregation** phenomena, that scrapie **prions** have been reported to modify the expression or localization of heat shock **proteins**, and that in **yeast**, propagation of a **prion**-like state (PSI+) depends on a heat shock (Hsp104) **protein**.

L2 ANSWER 3 OF 8 MEDLINE on STN
AN 1998057316 MEDLINE
DN PubMed ID: 9396609
TI The human 37-kDa laminin receptor precursor interacts with the **prion protein** in eukaryotic cells.
AU Rieger R; Edenhofer F; Lasmezas C I; Weiss S
CS Laboratorium fur Molekulare Biologie-Genzentrum-Institut fur Biochemie der LMU Munchen, Munich, Germany.
SO Nature medicine, **(1997 Dec)** Vol. 3, No. 12, pp. 1383-8.
Journal code: 9502015. ISSN: 1078-8956.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199801
ED Entered STN: 19980129
Last Updated on STN: 19980129
Entered Medline: 19980109
AB **Prions** are thought to consist of infectious **proteins** that cause transmissible spongiform encephalopathies. According to

overwhelming evidence, the pathogenic **prion protein** PrPSc converts its host encoded isoform PrPC into insoluble **aggregates** of PrPSc, concomitant with pathological modifications (for review, see refs. 1-3). Although the physiological role of PrPC is poorly understood, studies with PrP knockout mice demonstrated that PrPC is required for the development of **prion** diseases. Using the **yeast** two-hybrid technology in Saccharomyces cerevisiae, we identified the 37-kDa laminin receptor precursor (LRP) as interacting with the cellular **prion protein** PrPC. Mapping analysis of the LRP-PrP interaction site in S. cerevisiae revealed that PrP and laminin share the same binding domain (amino acids 161 to 180) on LRP. The LRP-PrP interaction was confirmed in vivo in insect (Sf9) and mammalian cells (COS-7). The LRP level was increased in scrapie-infected murine N2a cells and in brain and spleen of scrapie-infected mice. In contrast, the LRP concentration was not significantly altered in these organs from mice infected with the bovine spongiform encephalopathic agent (BSE), which have a lower PrPSc accumulation. LRP levels, however, were dramatically increased in brain and pancreas, slightly increased in the spleen and not altered in the liver of crapie-infected hamsters. These data show that enhanced LRP concentrations are correlated with PrPSc accumulation in organs from mice and hamsters. The laminin receptor precursor, which is highly conserved among mammals and is located on the cell surface, may act as a receptor or co-receptor for the **prion protein** on mammalian cells.

L2 ANSWER 4 OF 8 MEDLINE on STN
AN 97364830 MEDLINE
DN PubMed ID: 9219697
TI In vitro propagation of the **prion**-like state of **yeast** Sup35 **protein**.
AU Paushkin S V; Kushnirov V V; Smirnov V N; Ter-Avanesyan M D
CS Institute of Experimental Cardiology, Cardiology Research Center, 3rd Cherepkovskaya Street 15A, Moscow 121552, Russia.
SO Science, **(1997 Jul 18)** Vol. 277, No. 5324, pp. 381-3.
Journal code: 0404511. ISSN: 0036-8075.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199803
ED Entered STN: 19980407
Last Updated on STN: 20000303
Entered Medline: 19980323
AB The **yeast** cytoplasmically inherited genetic determinant [PSI+] is presumed to be a manifestation of the **prion**-like properties of the Sup35 **protein** (Sup35p). Here, cell-free conversion of Sup35p from [psi-] cells (Sup35ppsi-) to the **prion**-like [PSI+]-specific form (Sup35pPSI+) was observed. The conversion reaction could be repeated for several consecutive cycles, thus modeling in vitro continuous [PSI+] propagation. Size fractionation of lysates of [PSI+] cells demonstrated that the converting activity was associated solely with Sup35pPSI+ **aggregates**, which agrees with the nucleation model for [PSI+] propagation. Sup35pPSI+ was purified and showed high conversion activity, thus confirming the **prion** hypothesis for Sup35p.

L2 ANSWER 5 OF 8 MEDLINE on STN
AN 97338067 MEDLINE
DN PubMed ID: 9192614
TI **Prion**-inducing domain 2-114 of **yeast** Sup35 **protein** transforms in vitro into amyloid-like filaments.
AU King C Y; Tittmann P; Gross H; Gebert R; Aebi M; Wuthrich K
CS Institut fur Molekularbiologie und Biophysik, Eidgenossische Technische Hochschule, CH-8093 Zurich, Switzerland.

SO Proceedings of the National Academy of Sciences of the United States of America, **(1997 Jun 24)** Vol. 94, No. 13, pp. 6618-22.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199707
ED Entered STN: 19970805
Last Updated on STN: 19970805
Entered Medline: 19970721
AB The **yeast** non-Mendelian genetic factor [PSI], which enhances the efficiency of tRNA-mediated nonsense suppression in Saccharomyces cerevisiae, is thought to be an abnormal cellular isoform of the Sup35 **protein**. Genetic studies have established that the N-terminal part of the Sup35 **protein** is sufficient for the genesis as well as the maintenance of [PSI]. Here we demonstrate that the N-terminal polypeptide fragment consisting of residues 2-114 of Sup35p, Sup35pN, spontaneously **aggregates** to form thin filaments in vitro. The filaments show a beta-sheet-type circular dichroism spectrum, exhibit increased protease resistance, and show amyloid-like optical properties. It is further shown that filament growth in freshly prepared Sup35pN solutions can be induced by seeding with a dilute suspension of preformed filaments. These results suggest that the abnormal cellular isoform of Sup35p is an amyloid-like **aggregate** and further indicate that seeding might be responsible for the maintenance of the [PSI] element in vivo.

L2 ANSWER 6 OF 8 MEDLINE on STN
AN 97265414 MEDLINE
DN PubMed ID: 9111351
TI Interaction between **yeast** Sup45p (eRF1) and Sup35p (eRF3) polypeptide chain release factors: implications for **prion** -dependent regulation.
AU Paushkin S V; Kushnirov V V; Smirnov V N; Ter-Avanesyan M D
CS Institute of Experimental Cardiology, Cardiology Research Center, Moscow, Russia.
SO Molecular and cellular biology, **(1997 May)** Vol. 17, No. 5, pp. 2798-805.
Journal code: 8109087. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199705
ED Entered STN: 19970523
Last Updated on STN: 20030207
Entered Medline: 19970515
AB The SUP45 and SUP35 genes of Saccharomyces cerevisiae encode polypeptide chain release factors eRF1 and eRF3, respectively. It has been suggested that the Sup35 **protein** (Sup35p) is subject to a heritable conformational switch, similar to mammalian **prions**, thus giving rise to the non-Mendelian [PSI+] nonsense suppressor determinant. In a [PSI+] state, Sup35p forms high-molecular-weight **aggregates** which may inhibit Sup35p activity, leading to the [PSI+] phenotype. Sup35p is composed of the N-terminal domain (N) required for [PSI+] maintenance, the presumably nonfunctional middle region (M), and the C-terminal domain (C) essential for translation termination. In this study, we observed that the N domain, alone or as a part of larger fragments, can form **aggregates** in [PSI+] cells. Two sites for Sup45p binding were found within Sup35p: one is formed by the N and M domains, and the other is located within the C domain. Similarly to Sup35p, in [PSI+] cells Sup45p was found in **aggregates**. The **aggregation** of Sup45p is caused by its binding to Sup35p and was

not observed when the **aggregated** Sup35p fragments did not contain sites for Sup45p binding. The incorporation of Sup45p into the **aggregates** should inhibit its activity. The N domain of Sup35p, responsible for its **aggregation** in [PSI+] cells, may thus act as a repressor of another polypeptide chain release factor, Sup45p. This phenomenon represents a novel mechanism of regulation of gene expression at the posttranslational level.

L2 ANSWER 7 OF 8 MEDLINE on STN
AN 96325424 MEDLINE
DN PubMed ID: 8662547
TI Support for the **prion** hypothesis for inheritance of a phenotypic trait in **yeast**.
AU Patino M M; Liu J J; Glover J R; Lindquist S
CS Howard Hughes Medical Institute and the Department of Molecular Genetics and Cell Biology, University of Chicago, 5841 South Maryland Avenue, Chicago, IL 60637, USA.
NC GM25874 (NIGMS)
SO Science, **(1996 Aug 2)** Vol. 273, No. 5275, pp. 622-6.
Journal code: 0404511. ISSN: 0036-8075.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199609
ED Entered STN: 19960912
Last Updated on STN: 20021031
Entered Medline: 19960903
AB A cytoplasmically inherited genetic element in **yeast**, [PSI+], was confirmed to be a prionlike **aggregate** of the cellular **protein** Sup35 by differential centrifugation analysis and microscopic localization of a Sup35-green fluorescent **protein** fusion. **Aggregation** depended on the intracellular concentration and functional state of the chaperone **protein** Hsp104 in the same manner as did [PSI+] inheritance. The amino-terminal and carboxy-terminal domains of Sup35 contributed to the unusual behavior of [PSI+]. [PSI+] altered the conformational state of newly synthesized **prion** **proteins**, inducing them to **aggregate** as well, thus fulfilling a major tenet of the **prion** hypothesis.

L2 ANSWER 8 OF 8 MEDLINE on STN
AN 96272172 MEDLINE
DN PubMed ID: 8670813
TI Propagation of the **yeast** **prion**-like [psi+] determinant is mediated by oligomerization of the SUP35-encoded polypeptide chain release factor.
AU Paushkin S V; Kushnirov V V; Smirnov V N; Ter-Avanesyan M D
CS Institute of Experimental Cardiology, Cardiology Research Center, Moscow, Russia.
SO The EMBO journal, **(1996 Jun 17)** Vol. 15, No. 12, pp. 3127-34.
Journal code: 8208664. ISSN: 0261-4189.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199608
ED Entered STN: 19960911
Last Updated on STN: 20000303
Entered Medline: 19960827
AB The Sup35p **protein** of **yeast** Saccharomyces cerevisiae is a homologue of the polypeptide chain release factor 3 (eRF3) of higher eukaryotes. It has been suggested that this **protein** may adopt a specific self-propagating conformation, similar to mammalian **prions**, giving rise to the [psi+] nonsense suppressor determinant,

inherited in a non-Mendelian fashion. Here we present data confirming the **prion**-like nature of [psi+]. We show that Sup35p molecules interact with each other through their N-terminal domains in [psi+], but not [psi-] cells. This interaction is critical for [psi+] propagation, since its disruption leads to a loss of [psi+]. Similarly to mammalian **prions**, in [psi+] cells Sup35p forms high molecular weight **aggregates**, accumulating most of this **protein**. The **aggregation** inhibits Sup35p activity leading to a [psi+] nonsense-suppressor phenotype. N-terminally altered Sup35p molecules are unable to interact with the [psi+] Sup35p isoform, remain soluble and improve the translation termination in [psi+] strains, thus causing an antisuppressor phenotype. The overexpression of Hsp104p chaperone **protein** partially solubilizes Sup35P **aggregates** in the [psi+] strain, also causing an antisuppressor phenotype. We propose that Hsp104p plays a role in establishing stable [psi+] inheritance by splitting up Sup35p **aggregates** and thus ensuring equidistribution of the **prion**-like Sup35p isoform to daughter cells at cell divisions.

=>